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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/830,288	04/25/2001	Herwig Buchholz	MERCK 1943	7732

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EXAMINER	
KWON, BRIAN YONG S	
ART UNIT	**PAPER NUMBER**
1614	14

DATE MAILED: 11/04/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/830,288	Applicant(s) BUCHHOLZ ET AL.	
	Examiner Brian S Kwon	Art Unit 1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 September 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4,6-11,13-19 and 21-28* is/are pending in the application.

4a) Of the above claim(s) *7-11, 13 and 24-28* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4,6 and 14-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status of Application

1. A Request for Continued Examination (RCE) under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for Request for Continued Examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on September 08, 2003 has been entered.

2. It is noted that applicant originally has received an action on the merits for the Group I Invention, drawn to a composition, as being recorded in Paper No. 8. Accordingly, claims 7-11, 13 and 24-28 which are directed to a method claims are withdrawn from consideration as being directed a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03. Currently claims 1, 4, 6 and 14-23 are currently pending for prosecution on the merits.

It is noted to applicants that the examiner had required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.**

Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

3. The rejection of claims 1, 5-6, 14-16, 20 and 22 under 35 USC 102(b) as being anticipated by McGee (US 5198216) and the rejection of claims 1, 2, 5-6, 14, 16, 20 and 22 under 35 USC 102(b) as being anticipated by Lockett (US 5626884) will not be maintained in light of amendment filed July 7, 2003.

4. Claims 21-23 are rejected under 35 U.S.C. 112, second paragraph.

5. Claims 1, 4, 6 and 14-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Koppel et al. (US 5358720) in view of Bailey et al. (US 5997915).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 21-23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 21 and 23 recite the limitation "(6S)-tetrahydrofolic acid; 5-methyl-(6S)-tetrahydrofolic acid; 5-formyl-(6S)-tetrahydrofolic acid; 10-formyl-(6R)-tetrahydrofolic acid; 5,10-methylene-(6R)-tetrahydrofolic acid; 5,10-methenyl-(6R)-tetrahydrofolic acid; and their physiologically acceptable salts" and "5-methyl-(6S)-tetrahydrofolic acid" in claim 1 respectively. There is insufficient antecedent basis for this limitation in the claim.

Claim 22 which is a dependent claim of claim 1 recite that component B comprises one or more compounds selected from the group consisting of derivatives of L- and S-glutamic acid. In other words, any derivatives of L- and S-glutamic acid (having methyl transporter activity) can be used as the component B in said composition. However, the claimed component B in claim 1 only limits to "dihydrofolic acid, tetrahydrofolic acid, 5-methyltetrhydrofolic acid, 5-formyltetrahydrofolic acid, 10-formyltetrahydrofolic acid, 5,10-methylenetetrahydrofolic acid, and 5,10-methenyltetrahydrofolic acid, and physiologically acceptable salt thereof". Claim 22 is not clear whether derivatives of L-and S-glutamic acid refers to derivatives of L- and S-glutamic

acid of "dihydrofolic acid, tetrahydrofolic acid, 5-methyltetrhydrofolic acid, 5-formyltetrahydrofolic acid, 10-formyltetrahydrofolic acid, 5,10-methylenetetrahydrofolic acid, and 5,10-methenyltetrahydrofolic acid, and physiologically acceptable salt thereof" or any derivatives of L- and S-glutamic acid. It appears that the scope of dependent claim 22 is broader than the parent claim 1 and such inconsistency in the scope of the claimed subject matter renders the claimed invention vague and indefinite.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any

evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 1, 4, 6 and 14-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Koppel (US 5358720) in view of Bailey et al. (US 5997915).

Koppel discloses a multivitamin-multimineral supplement composition comprising (a) methyl or methylene donor such as choline or betaine (in salt form), (b) methyl transporter such as folic acid (synonym: pteroyl-L-glutamic acid), (c) citrus bioflavonoid, hesperiden complex and rutin (column 3, line 48 thru column 4, line 54).

Bailey teaches or suggests the advantage of substituting folic acid with the natural isomer of tetrahydrofolic acid or a derivatives including 5-methyl-(6S)-tetrahydrofolic acid for the satisfaction or partial satisfaction of the dietary requirement for the multivitamine preparation; for the accommodation of patient's needs where folic acid bioavailability is poor; and the advantage of providing more choices to health care professionals in recommending optimal levels when a more uniformly absorbed form of folate is widely used (column 6, line 65 thru column 7, line 18).

The teaching of Koppel differs from the claimed invention in (i) the use of folic acid derivatives, namely 5-methyltetrahydrofolic acid, more specifically 5-methyl-(6S)-tetrahydrofolic acid (required in claims 1, 4, 6 and 14-23) ; (ii) "lyophilized" (required in claim 17); and (iii) the specific molar ratio of each components in said composition (required in claim 18).

To incorporate such teaching regarding the use of folic acid derivatives such as 5-methyltetrahydrofolic acid (or 5-methyl-(6S)-tetrahydrofolic acid) into the teaching of Koppel, would have been obvious in view of Bailey who teaches or suggests the advantage of using the natural isomer of tetrahydrofolic acid such as 5-methyl-(6S)-tetrahydrofolic acid in improving poor bioavailability or non-uniformly absorbed characteristic of folic acid.

One having ordinary skill in the art would have been motivated to make such modification to accommodate the needs of those for whom folic acid bioavailability is poor and to accommodate patient's preference where the compliance could be improved with more uniformly absorbed form of folate.

With respect to the limitation of "lyophilized", such determination is well considered within the skill of the artisan since the freeze-drying method is routinely utilized in pharmaceutical formulation art. Since the prior art as a whole fairly teaches or suggests the formulation of said composition in tablet, capsule and liquid, one skilled in the art at the time of applicant's invention would have been motivated to prepare said composition in "lyophilized" or freeze-dried.

Furthermore, optimization of known active ingredients in a composition is well considered within the skill in the art, and the artisan would be motivated to determine optimum amounts to get the maximum effect of the drug. Hence, the reference makes obvious the instant invention.

Conclusion

8. No claim is allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Kwon whose telephone number is (703) 308-5377. The examiner can normally be reached Tuesday through Friday from 9:00 am to 7:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marianne Seidel, can be reached on (703) 308-4725. The fax number for this Group is (703) 308-4556.

Any inquiry of a general nature of relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-1235.

Brian Kwon

ZOHREH FAY
PRIMARY EXAMINER
GROUP 1600

Zahreh Fay